

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-20. (Cancelled)

21. (New) A method for increasing neuron survival in a patient having a neurodegenerative ocular disease, the method comprising administering to the patient an effective amount of a PDE4 inhibitor compound from the pyrazolopyridine family.

22. (New) The method of claim 21, for inhibiting or reducing neuron death due to excitotoxicity during neurodegenerative ocular diseases.

23. (New) The method of claim 21, wherein the compound is also a ligand of the peripheral benzodiazepine receptor (PBR).

24. (New) The method of claim 21, wherein the compound is also a ligand of GABA receptors of the type GABA(A).

25. (New) The method of claim 21, wherein the compound is selected in the group consisting of etazolate and tracazolate, preferably etazolate.

26. (New) The method of claim 21, wherein the compound is selected in the group consisting of the following compounds :

4-butylamino-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

1-(4-amino-pyrazolo[3,4-*b*]pyridin-1-yl)- β -*D*-1-deoxy-ribofuranose,

1-ethyl-4-(*N*'-isopropylidene-hydrazino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester (SQ 20009),

4-amino-6-methyl-1-*n*-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine,

4-amino-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester (desbutyl tracacolate),

4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

1-ethyl-6-methyl-4-methylamino-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

4-amino-6-methyl-1-propyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

1-ethyl-4-ethylamino-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

4-amino-1-butyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

5-(4-amino-pyrazolo[3,4-*b*]pyridin-1-yl)-2-hydroxymethyl-tetrahydro-furan-3-ol,

1-allyl-4-amino-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-6-methyl-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid,

4-amino-1-ethyl-3,6-dimethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

4-dimethylamino-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl
ester,

1-ethyl-6-methyl-4-propylamino-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

4-amino-6-methyl-1-pent-4-ynyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

4-amino-1-but-3-enyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-allylamide,

4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-isopropylamide,

4-amino-1-pentyl-N-n-propyl-1*H*-pyrazolo-[3,4-*b*]pyridine-5-carboxamide,

4-amino-1-butyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-6-methyl-1-pent-3-ynyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-prop-2-ynylamide,

4-amino-1-(3-methyl-butyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-1-pentyl-1*H*-pyrazolo<3,4-*b*>pyridine-5-N-(2-propenyl)carboxamide,

4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-butylamide,

4-amino-1-but-3-ynyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-1-but-3-enyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-6-methyl-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-allylamide,

4-amino-6-methyl-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-6-methyl-1-(3-methyl-butyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-6-methyl-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid isobutyl ester,

4-amino-6-methyl-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-butylamide,

4-amino-6-methyl-1-(3-methyl-but-2-enyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-cyclopropylamide,

ethyl 4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-hydroxamate,

4-amino-6-methyl-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid prop-2-ynyl ester,

4-amino-6-methyl-1-pent-4-ynyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-6-methyl-1-pent-4-enyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-1-pent-3-ynyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-propylamide,

4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-cyclopropylmethyl-amide,

4-amino-6-methyl-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid 2-methyl-allyl ester,

4-amino-1-pent-3-ynyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-allylamide (ICI 190,622),

4-amino-1-pent-4-ynyl-N-2-propenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

4-amino-1-pent-3-ynyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-prop-2-ynylamide,

4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-but-2-ynylamide,

4-amino-6-methyl-1-pent-3-ynyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-1-(2-cyclopropyl-ethyl)-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-1-hex-5-ynyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid allyl ester,

4-amino-1-pent-3-ynyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-cyclopropylmethyl-amide,

4-amino-6-methyl-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid but-3-enyl
ester,

4-amino-6-methyl-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid
cyclopropylmethyl ester,

4-butylamino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-allylamide,

4-amino-6-methyl-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid 2-cyclopropyl-
ethyl ester,

4-amino-6-methyl-1-pent-3-ynyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid
cyclopropylmethyl ester,

4-amino-6-methyl-1-pent-4-ynyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid
cyclopropylmethyl ester,

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4-amino-1-benzyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-benzylamide,

4-amino-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-phenylamide,

4-amino-6-methyl-1-pentyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid benzyl ester,

4-azido-1-β-D-ribofuranosylpyrazolo[3,4-*b*]pyridine,

1-pent-3-ynyl-N-2-propenyl-4-propionamido-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

2-(4-amino-pyrazolo[3,4-*b*]pyridin-1-yl)-5-hydroxymethyl-tetrahydro-furan-3,4-diol,

2-(6-methyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)-ethanol,

3-(6-methyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)-propan-1-ol;

3-(6-methyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)-acetic acid propyl ester,

2-(6-methyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)-propionic acid ethyl ester,

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2-(6-methyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)-pentanoic acid ethyl ester,

2-(6-methyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)-benzoic acid ethyl ester,

3-(6-methyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)-pentanoic acid propyl ester,

N-benzylidene-*N*-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-hydrazine,

N-furan-2-ylmethylene-*N*-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-hydrazine,

N-(4-fluoro-benzylidene)-*N*-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-
hydrazine,

N-(3-furan-2-yl-allylidene)-*N*-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-
hydrazine,

N-(4-methoxy-benzylidene)-*N*-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-
hydrazine,

4-[(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-hydrazonomethyl]-benzonitrile,

N-benzo[1,3]dioxol-5-ylmethylene-*N'*-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-hydrazine,

N-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-*N'*-(4-nitro-benzylidene)-hydrazine,

N-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-*N'*-(2-nitro-benzylidene)-hydrazine,

N-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-*N'*-(4-trifluoromethyl-benzylidene)-hydrazine,

N-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-*N'*-(5-nitro-furan-2-ylmethylene)-hydrazine,

N-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-*N'*-(2-trifluoromethyl-benzylidene)-hydrazine,

N-(3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-*N'*-(6-nitro-benzo[1,3]dioxol-5-ylmethylene)-hydrazine,

4-(3-chloro-4-methoxy-benzylamino)-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid,

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4-(3-chloro-4-methoxy-benzylamino)-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5- (pyridin-4-ylmethyl)-amide,

4-(3-chloro-4-methoxy-benzylamino)-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5- (tetrahydro-furan-2-ylmethyl)-amide,

4-(3-chloro-4-methoxy-benzylamino)-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5- (5-hydroxy-pentyl)-amide,

4-(3-chloro-4-methoxy-benzylamino)-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-[3-(2-oxo-pyrrolidin-1-yl)-propyl]-amide,

4-*tert*-butylamino-1-(2-chloro-2-phenyl-ethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

1-(2-chloro-2-phenyl-ethyl)-4-cyclopropylamino-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

1-(2-chloro-2-phenyl-ethyl)-4-propylamino-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

1-(2-chloro-2-phenyl-ethyl)-4-phenylamino-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

4-butylamino-1-(2-chloro-2-phenyl-ethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

1-(2-chloro-2-phenyl-ethyl)-4-(2-ethoxy-ethylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester,

4-benzylamino-1-(2-chloro-2-phenyl-ethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester, and

1-(2-chloro-2-phenyl-ethyl)-4-phenethylamino-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid ethyl ester.

27. (New) The method of claim 21, wherein the compound is an antisense nucleic acid inhibiting the transcription of the PDE4B gene or the translation of the corresponding messenger.

28. (New) The method of claim 21, wherein the patient suffers from retinal degeneration.

29. (New) The method of claim 21, wherein the patient suffers from retinitis pigmentosa, age-related macular degeneration, or the retinal effects of glaucoma or a retinopathy.

30. (New) A method for treating a neurodegenerative ocular disease in a subject, the method comprising administering to a subject in need thereof an effective amount of etazolate.

31. (New) A method for increasing neuron survival in a patient having a neurodegenerative ocular disease, the method comprising administering to the patient an effective amount of etazolate.

32. (New) A method of claim 30, wherein the neurodegenerative ocular disease is retinitis pigmentosa.

33. (New) A method of claim 30, wherein the neurodegenerative ocular disease is age-related macular degeneration.

34. (New) A method of claim 30, wherein the neurodegenerative ocular disease is the effect on retinal neurons of the presence and the evolution of glaucoma.

35. (New) A method of claim 30, wherein the neurodegenerative ocular disease is a retinopathy.

36. (New) A method of claim 30, wherein etazolate is administered in oral form.

37. (New) A pharmaceutical composition comprising a compound selected in the group consisting of etazolate and tracazolate, and a pharmaceutically acceptable excipient allowing retro- and/or intra-ocular administration.

38. (New) A method for detecting a situation of excitotoxicity or neuronal stress in a subject, comprising measuring *in vitro* the expression of AKAP1 and/or GABA(A)RAPL1 in a sample from the subject, or detecting the presence of a mutant form of AKAP1 and/or GABA(A)RAPL1 RNA in said sample.

39. (New) A method for the selection, identification or characterization of compounds active against neurodegenerative ocular pathologies, comprising contacting a test compound with PDE4B, AKAP1 and/or GABA(A)RAPL1, or with a cell expressing same, and selecting, identifying or characterizing a compound binding to said protein or

inhibiting the expression or activity of said protein, said binding or inhibition being indicative of compounds active against neurodegenerative ocular pathologies.

40. (New) The method of claim 39, wherein said PDE4B is a PDE4B variant devoid of the 3' non-coding region.